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SERIAL NUMBER	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
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07/957,646 10/28/92 STAVRIANOPOLLOU

LEN2/0105

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1 EN77(C2) /
EXAMINER

MARSCHER, A

ART UNIT PAPER NUMBER

19

1807

DATE MAILED:

01/05/93

This is a communication from the examiner in charge of your application.
COMMISSIONER OF PATENTS AND TRADEMARKS

☒ This application has been examined ☒ Responsive to communication filed on 9-2-94
10-28-94 ☐ This action is made final.

A shortened statutory period for response to this action is set to expire 3 month(s), 0 days from the date of this letter.
Failure to respond within the period for response will cause the application to become abandoned. 35 U.S.C. 133

Part I THE FOLLOWING ATTACHMENT(S) ARE PART OF THIS ACTION:

- ☒ Notice of References Cited by Examiner, PTO-892.
- ☒ Notice of Art Cited by Applicant, PTO-1449. (1 sheet)
- ☐ Information on How to Effect Drawing Changes, PTO-1474.
- ☐ Notice of Draftsman's Patent Drawing Review, PTO-948.
- ☐ Notice of Informal Patent Application, PTO-152.
- ☒ Ex. Int. Sum. of 9-23-94, Page #16

Part II SUMMARY OF ACTION

- ☒ Claims 27-47 are pending in the application.
Of the above, claims _____ are withdrawn from consideration.
- ☒ Claims 1-26 have been cancelled.
- ☐ Claims _____ are allowed.
- ☒ Claims 27-47 are rejected.
- ☐ Claims _____ are objected to.
- ☐ Claims _____ are subject to restriction or election requirement.
- ☐ This application has been filed with informal drawings under 37 C.F.R. 1.85 which are acceptable for examination purposes.
- ☐ Formal drawings are required in response to this Office action.
- ☐ The corrected or substitute drawings have been received on _____. Under 37 C.F.R. 1.84 these drawings are ☐ acceptable; ☐ not acceptable (see explanation or Notice of Draftsman's Patent Drawing Review, PTO-948).
- ☐ The proposed additional or substitute sheet(s) of drawings, filed on _____, has (have) been ☐ approved by the examiner; ☐ disapproved by the examiner (see explanation).
- ☐ The proposed drawing correction, filed _____, has been ☐ approved; ☐ disapproved (see explanation).
- ☐ Acknowledgement is made of the claim for priority under 35 U.S.C. 119. The certified copy has ☐ been received ☐ not been received ☐ been filed in parent application, serial no. _____; filed on _____.
- ☐ Since this application appears to be in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under Ex parte Quayle, 1935 C.D. 11; 453 O.G. 213.
- ☐ Other

EXAMINER'S ACTION

Applicants' arguments, filed 9/2/94, have been fully considered and they are deemed to be persuasive to overcome the rejections set forth in the office action, mailed 7/25/94. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are newly applied. They constitute the complete set presently being applied to the instant application.

Due to the withdrawal of the previously applied rejections, the finality of the office action, mailed 7/25/94, is hereby withdrawn.

The proposed amendments, filed as after final amendments on 9/2/94 and 10/28/94, have both been denied entry because both proposed amendments contain NEW MATTER as discussed below.

The NEW MATTER in the 9/2/94 amendment is in the title wherein a "COMPOSITION EMPLOYING..." is given which discloses the broad scope of a composition limited only in that it contains a chemically labeled oligonucleotide or polynucleotide. This is NEW MATTER for two reasons. Firstly, there are no broadly defined compositions as such as filed nor even a written description of "composition" as filed. Secondly, only oligonucleotide or polynucleotide "probes" are labeled as filed. One interpretation of the title is that, since analytes of the invention may be either polynucleotides or oligonucleotides, the labeling may be directly incorporated in the analyte. No such directly labeled analytes are disclosed as filed. The labeling in the disclosure as filed "only" occurs via a fixed

polynucleotide analyte that is hybridized to a labeled polynucleotide probe. This prevention of NEW MATTER inclusion via the proposed title also corresponds to the NEW MATTER discussed below regarding the claims.

The NEW MATTER in the claims proposed 10/28/94 is directed to a lack of written description of systems as filed. There is no system, disclosed as filed, that contains specifically two parts; one part being a probe and the other being a solid support. For example, a thorough review of the "SUMMARY OF THE INVENTION" section starting on page 9 reveals that methods are disclosed until page 14, first full paragraph. In summary, said page 14 paragraph set forth three embodiments as follows: 1) a device containing a fluid retaining portion which portion contains an immobilized polynucleotide hybridized to a polynucleotide or oligonucleotide probe with a chemical label plus a soluble signal; 2) an apparatus comprising a plurality of said devices; 3) a non-porous solid support to which a polynucleotide is directly fixed in hybridizable form to which a covalently chemically labeled polynucleotide may be hybridized. It is noted that claims 20-26, as filed, do not go beyond the scope of the above summarized page 14. Lastly, the last paragraph of the specification on page 25 suggests many alterations, modifications, and substitutions. These suggestions are deemed to be implied limitations that do not meet the written description requirement of 35 U.S.C. § 112, first paragraph. The last sentence on page 25 clearly defines the scope of the

invention as being limited by the claims as filed. None of the above disclosures as filed supply written description of the system of proposed claims 48-68 regarding the specific probe plus solid support given as a two component system. Also, the open claim language term "comprises" in line 2 of claim 48 is broader than the third embodiment given in the specification on page 14 or claims 24-26, as filed, in that at the very least a polynucleotide is always fixed on the solid support as cited in claim 24 as filed. Labeled supports containing both the polynucleotide of claim 24 plus a chemically labeled probe is then the subject matter of claim 25, as filed. In summary, the scope of the above cited "comprises" is broader than the only similar embodiments where "at least" a polynucleotide is fixed onto the support with labeling only via the hybridization of a chemically labeled probe. Numerous other NEW MATTER limitations are present in the 10/28/94 amendment. For example, a separate solid support with no limitations regarding porosity or transparency as a "subelement" in a non-porous transparent system etc. is not disclosed in the above summarized disclosure as filed as now proposed in claims 48 and 49. The "same" or "different" materials limitations of claims 53 and 54 have not been found as filed. The apparatus of claim 68 is not limited to a "plurality of devices" as are all of the apparatus disclosures as filed. In summary, the proposed amendment filed 10/28/94 contains many NEW MATTER disclosures that are have no written description in the instant application as filed.

If applicant desires priority under 35 U.S.C. § 120 based upon a parent application, specific reference to the parent application must be made in the instant application. It is noted that this appears as the first sentence of the specification following the title, preferably as a separate paragraph. Status of the parent application (whether patented or abandoned) should also be included. If a parent application has become a patent, the expression "Patent No." should follow the filing date of the parent application. If a parent application has become abandoned, the expression "abandoned" should follow the filing date of the parent application.

The above paragraph is appropriate because in the cross reference to other related applns the app # 07/607,347 should have been listed as having been abandoned.

The citation directed to Kourilsky et al. (P/N 4,581,333) on the enclosed PTO Form 1449 is lined through to avoid duplication of citation because it is already of record as having been considered in the IDS, filed 6/2/94.

The following is a quotation of the first paragraph of 35 U.S.C. § 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The specification is objected to under 35 U.S.C. § 112, first paragraph, as the disclosure, as originally filed, does not provide support for the invention as is now claimed.

The preliminary amendment, filed 10/28/92, has been filed in a continuation application therefore any added disclosure therein is NEW MATTER compared to the earlier filed application of which the instant one is a continuation. Claim 27 contains NEW MATTER

in that a composition is therein cited without "composition" being defined or given in a written description as filed. Additionally, the claimed composition is cited in claim 27 as comprising a system discussed above as containing NEW MATTER. Also, comparing claims 24-26 as filed to claim 27, it is clear that a solid support with polynucleotide with or without a hybridized and chemically labeled polynucleotide or oligonucleotide probe is the scope of the instant invention and not a composition "comprising" a "system" which further comprises a double-stranded oligonucleotide or polynucleotide. These three layers of subject matter go far beyond claim 24, for example, as filed, and therefore are deemed to contain NEW MATTER. Also claims 27 and 28 contain NEW MATTER similar to claims 48 and 49 as discussed above regarding a solid support subelement in a system. The "same" or "different" limitations of claims 34 and 35 have not been found as filed as also the sandwich type formats of claims 36 and 37. Similarly, the limitation directed to direct or indirect attachment of signalling moiety to the chemical label of claim 42 is NEW MATTER as being a separate limitation from that of claim 41. The apparatus of claim 46 is not limited to a "plurality of devices" as are all of the apparatus disclosures as filed. In summary, the preliminary amendment filed 10/28/92 contains many NEW MATTER disclosures in claims 27-47 that are have no written description in the instant application as filed.

Claims 27-47 are rejected under 35 U.S.C. § 112, first

paragraph, for the reasons set forth in the objection to the specification.

Claims 31-33 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 31 is unclear in that what appears to be a Markush group lists plastic as well as polystyrene, dextran, and polypropylene because polystyrene, dextran, and polypropylene are plastics. What are the metes and bounds of the claim unless it is merely is inclusive of plastics?

Claims 32 and 33 are vague and indefinite in that the cooperativity between the members listed therein and the solid support of the "system" is not defined. Seemingly the cited members of claims 32 and 33 are meant to be options for the solid support of claim 27 but this is not clearly defined as such. Could applicants mean the solid support and the members to be separate components of the claimed system? Clarification is requested as to the metes and bounds and relationships of the components of the claimed "system".

Claims 44 and 45 are rejected under 35 U.S.C. § 112, fourth paragraph, as being of improper dependent form for failing to further limit the subject matter of a previous claim.

Claims 44 and 45 cite the generation of a soluble signal which does not further limit claim 27 where only the "capability" of generating such as signal is cited. The generation of such a

signal does not further limit the composition of claim 27 from which claims 44 or 45 ultimately depends.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

Claims 27-31, 34-36, 38, 39, and 41-45 are rejected under 35 U.S.C. § 102(e) as being clearly anticipated by Stuart et al.

Stuart et al. disclose the formation of DNA-RNA hybrids by in situ hybridization performed on microscope slides wherein the hybrids are detected by antibody binding to said hybrids starting in column 4, line 1, and proceeding through the section entitled "EXPERIMENTAL". Several types of antibody label types are given in Stuart et al. in column 4, lines 37-55, inclusive of enzymes such as horseradish peroxidase. These disclosures read on the above listed instant claims. It is additionally noted that microscope slides are non-porous and transparent and are disclosed as being viewed by light microscopy as summarized in column 6, lines 17-26, thus also inclusive of a "system" as instantly claimed. Such a light microscope system includes non-

porous transparent elements which are interpretable as reading on these limitations of the system of the instant claims. It is also noted that Stuart et al. reads on the above listed instant claims after removal of the NEW MATTER discussed above. The above listed claims contain the limitation directed to "a signalling moiety which is capable of generating a soluble signal". Enzymes such as horseradish peroxidase inherently are "capable of generating a soluble signal" as is well known in the peroxidase labeled antibody art. It is acknowledged that Stuart et al. does not disclose the actual generation of a soluble signal. This lack of actual soluble signal generation is, however, not deemed to prevent this rejection because the claims are composition claims citing only the "capability" of generating such a soluble signal. The inherency of this "capability" has been discussed above.

Claims 27-31, 34-36, 38, 39, and 41-45 are rejected under 35 U.S.C. § 102(a) as being clearly anticipated either by Langer-Safer et al. or Manuelidis et al.

The listed claims are anticipated either by Langer-Safer et al. or Manuelidis et al. in the same manner as the above rejection based on Stuart et al. because both references also perform in situ hybridization of chromosome spreads on microscope slides etc. as summarized above. It is noted that Langer-Safer et al. has been listed on a PTO Form 1449, filed by applicants on 6/2/94, as Langer et al. (1982) as given in PNAS, volume 79, pages 4381-4385. The correct citation is to Langer-Safer et al. and

has also been corrected on the PTO Form 1449.

Claims 27-31, 34-36, and 38-45 are rejected under 35 U.S.C. § 102(e) as being anticipated by Ward et al.

Ward et al. disclose via the "GENERAL PROTOCOL" and with connected discussion elsewhere at the bottom of columns 19 and 20 in situ hybridization where immobilized double-stranded nucleic acid is shown visualized with a biotinylated probe bound to avidin-peroxidase. This reads on the listed claims as does the above disclosures directed to in situ hybridization but also covering biotin-avidin mediated embodiments.

Claims 32, 33, 37, 46, and 47 are allowable over the prior art of record because the prior art of record does not teach or suggest the well, tube, or cuvette practice as solid supports for enzyme labeled hybridization nor sandwich hybridization nor apparatus or kits for performing a method as previously allowed in Patent Number 4,994,373.

No claim is allowed.

Papers related to this application may be submitted to Group 1800 by facsimile transmission. Papers should be faxed to Group 1800 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989).

The CM1 Fax Center number is either (703) 305-3014 or (703) 308-4227.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ardin Marschel, Ph.D., whose telephone number is (703) 308-3894. The examiner can normally be reached on Monday-Friday from 8 A.M. to 4 P.M.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Margaret Parr, can be reached on (703) 308-2454.

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Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

AM
A. MARSCHEL:am

December 16, 1994

M. Parr 12-19-94
MARGARET PARR
SUPERVISORY PATENT EXAMINER
GROUP 1800